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Set	Items	Description
S1	6	S HIV (S) TAT (S) VACCIN? (S) MICROPARTICL?
S2	3	RD (unique items)
S3	0	S S1 NOT PY>2003
S4	6	S HIV (S) TAT (S) MICROPARTICL?
S5	0	S S4 NOT PY>2003
S6	125	S HIV (S) VACCIN? (S) MICROPARTICL?
S7	65	S S6 NOT PY>2003
S8	22	RD (unique items)
S9	55	S HIV (S) ADSORB? (S) MICROPARTICL?
S10	25	S S9 NOT PY>2003
S11	7	RD (unique items)

Set	Items	Description
S1	0	S MICROPARTICLE? (S) (CORE? (4N) INSOLUBLE) (S) (SHELL? (4N) HYDROPHILIC) (S) (ANTIGEN? OR VACCINE? OR PROTEIN?)
S2	0	S PARTICLE? (S) (CORE? (6N) INSOLUBLE) (S) (SHELL? (6N) HYDROPHILIC) (S) (ANTIGEN? OR VACCINE? OR PROTEIN?)
S3	0	S PARTICLE? (S) CORE? (S) INSOLUBLE (S) SHELL? (S) HYDROPHILIC (S) (ANTIGEN? OR VACCINE? OR PROTEIN?)
S4	4	S PARTICLE? (S) (CORE? (6N) INSOLUBLE) (S) (SHELL? (6N) HYDROPHILIC)
S5	1	RD (unique items)
S6	8	S PARTICLE? (S) CORE? (S) INSOLUBLE (S) SHELL? (S) HYDROPHILIC
S7	7	S S6 NOT S5
S8	2	RD (unique items)

Micellar nanocarriers: pharmaceutical perspectives.

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Micelles, self-assembling nanosized colloidal particles with a hydrophobic core and hydrophilic shell are currently successfully used as pharmaceutical carriers for water-insoluble drugs and demonstrate a series of attractive properties as drug carriers. Among the micelle-forming compounds, amphiphilic copolymers, i.e., polymers consisting of hydrophobic block and hydrophilic block, are gaining an increasing attention. Polymeric micelles possess high stability both in vitro and in vivo and good biocompatibility, and can solubilize a broad variety of poorly soluble pharmaceuticals many of these drug-loaded micelles are currently at different stages of preclinical and clinical trials. Among polymeric micelles, a special group is formed by lipid- core micelles, i.e., micelles formed

by conjugates of soluble copolymers with lipids (such as polyethylene glycol-phosphatidyl ethanolamine conjugate, PEG-PE). Polymeric micelles, including lipid- core micelles, carrying various reporter (contrast) groups may become the imaging agents of choice in different imaging modalities. All these micelles can also be used as targeted drug delivery systems. The targeting can be achieved via the enhanced permeability and retention (EPR) effect (into the areas with the compromised vasculature), by making micelles of stimuli-responsive amphiphilic block-copolymers, or by attaching specific targeting ligand molecules to the micelle surface. Immunomicelles prepared by coupling monoclonal antibody molecules to p-nitrophenylcarbonyl groups on the water-exposed termini of the micelle corona-forming blocks demonstrate high binding specificity and targetability. This review will discuss some recent trends in using micelles as pharmaceutical carriers.

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Solubilization and controlled release of a hydrophobic drug using novel micelle-forming ABC triblock copolymers.

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Amphiphilic ABC triblock copolymers composed of monomethoxy-capped poly(ethylene glycol) (MPEG), poly(2-(dimethylamino)ethyl methacrylate) (DMA), and poly(2-(diethylamino)ethyl methacrylate) (DEA) have been synthesized by atom transfer radical polymerization (ATRP). These copolymers dissolve molecularly in acidic aqueous media at room temperature due to protonation of the tertiary amine groups on the DMA and DEA residues. On adjusting the pH with base, micellization occurred at pH 8, with the water-insoluble, deprotonated DEA block forming the hydrophobic cores and the MPEG and DMA blocks forming the hydrophilic micellar coronas and inner shells, respectively. This pH-induced micellization has been exploited to develop a solvent-free protocol for drug loading. A model hydrophobic drug, dipyrindamole (DIP), which dissolves in acid but is insoluble above pH 5.8, was incorporated into the micelles by increasing the pH of an aqueous drug/copolymer mixture to 9. Both the empty and the drug-loaded micelles were characterized by dynamic light scattering and fluorescence studies. The interaction of both pyrene and DIP with the MPEG-DMA-DEA micelles was studied by fluorescence; both compounds had relatively high partition coefficients into the micelles,  $4.5 \times 10^5$  and  $1.5 \times 10^4$ , respectively. Intensity-average micelle diameters ranged from 20 to 90 nm, depending on the polymer composition and concentration. Shorter MPEG blocks ( $M_n = 2000$ ) produced larger micelles than longer MPEG blocks ( $M_n = 5000$ ) due to the shift in the hydrophilic-hydrophobic balance of the copolymer.

Transmission electron microscopy studies of the drug-loaded micelles indicated spherical morphologies and reasonably uniform particle size distributions, which is in marked contrast to the needlelike morphology observed for pure DIP in the absence of the copolymer. Experiments on

controlled release demonstrated that DIP-loaded MPEG-DMA-DEA micelles act as a drug carrier, giving slow release to the surrounding solution over a period of days. Rapid release can be triggered by reducing the pH to reverse the micellization.